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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,621	10/06/2006	Maria Elena Ferrero	2503-1228	3886

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,621	FERRERO, MARIA ELENA	
	Examiner	Art Unit	
	LAWRENCE E. CRANE	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *January 12, 2009 (RCE & amendment)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,10,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 9, 10, 14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims **2-8, 11-13 and 16-17** have been cancelled, claims **1, 9, 14 and 15** have been amended, the disclosure and the abstract have not been further amended, and no new claims have been added as per the RCE and the amendment filed January 12, 2009. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of the Office action. Applicant has also filed a declaration filed under 37 C.F.R. §1.132 and signed by the applicant, Mme. Ferrero, on January 8, 2009.

Claims **1, 9-10 and 14-15** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claim **1** is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 3, the term "a cancer selected from lymphoma" is not a proper Markush group because there is only a single member in the group (applicant's comments to the contrary in applicant's response are noted, but the claim does not correspond thereto). Applicant is respectfully requested to delete the Markush preamble or make other appropriate amendment.

Applicant's arguments with respect to claim **1** have been considered but are deemed to be moot in view of the new grounds of rejection. Applicant's amendment necessitated this new grounds of rejection.

Claims **1, 9-10 and 14-15** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant disclosure has only provided two examples wherein the effectiveness of "o-ATP" in the inhibition of cell division of one class of endothelial cell is disclosed. This showing, together with the previous assertions of applicant's theory of the scope of the

pharmaceutical activity of o-ATP, is insufficient as a written description to support claims **1, 9-10 and 14-15** wherein o-ATP has been asserted by applicant to be active against a large number of generic disease conditions (all "lymphomas" and any disease wherein administration of o-ATP to cause "VEGF" inhibition is an effective treatment). Applicant's assertions are not deemed to support the now narrowed scope because of the presence of only a single direct test result showing that o-ATP has activity against what appears to be a single neoplastic cell line in vitro.. See *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991), a decision in its first part standing for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas (cancer and tumor treatments remain highly unpredictable particularly in the area of neoplasms of the nervous system and the pancreas) are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment. See the MPEP at §2107.03 for additional guidance concerning this policy.

Applicant's arguments filed January 12, 2009 have been fully considered but they are not persuasive.

Examiner has read and reviewed the declaration of Mme. Ferrero and finds that it adds a small amount of additional information to the instant disclosure, but does not provide an adequate basis to overcome the above rejection for the following reasons: i) the data presented does not disclose the treatment of a particular disease condition in a text host, and ii) the data represents only a single test exemplification. As noted in the newly cited Google search result, Ehrlich tumor is apparently generic for a number of different disease conditions, leading examiner to conclude that the above rejection remains valid because the two remaining independent claims, claims **1 and 9**, both claim generic disease classes and the data provided is not clearly connected to either disease class. For these reasons examiner has maintained the above rejection.

Claims **1, 9-10 and 14-15** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the inhibition of cell division of a single cell type by the administration of "[periodate] oxidized adenosine triphosphate," does not reasonably provide enablement for the treatment of any neoplastic or other disease condition wherein the inhibition of angiogenesis or any other effect caused by administration of -- po-ATP -- . The specification does not enable any person skilled in the art to which it pertains, or with which it

is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The instant claims are directed to the treatment of a vast array of generically defined disease conditions wherein VEGF-induced angiogenesis is effectively inhibited by administration of an effective amount of periodate oxidized ATP (po-ATP), and to pharmaceutical compositions wherein po-ATP is present in combination with a vast array of other medicinally active substances.

B. The nature of the invention: The invention is directed to treating diseases wherein angiogenesis is a necessary part of disease progression and therefore, according to the theory of the disclosure, the inhibition of angiogenesis by administration of po-ATP would be effective in treating the disease.

C. The state of the prior art: Following a review of the art of record it is clear that -- po-ATP -- (defined as the dialdehyde produced by periodate oxidation of ATP) is capable of interfering with certain purinergic receptors, but there is no disclosure in said prior art of the administration of po-ATP alone or in combination with other medicinally active substances to treat atherosclerosis, leukemia, or any other neoplastic disease condition except for lymphoma (Ehrlich's tumor cells) wherein angiogenesis is an essential part of disease development and/or disease progression over time.

D. The level of one of ordinary skill: The ordinary practitioner in the instant art area would be expected to have experience in medical practice and an understanding of biological sciences.

E. The level of predictability in the art: Predictability is inversely proportional to the knowledge of the ordinary practitioner concerning the treatment of the entire spectrum of the disease conditions claimed herein to be effectively treated. Neither the instant disclosure nor the prior art except for one newly cited reference (**Cory et al.**) provide any guidance

concerning how to practice the instant claimed method of treatment, thereby rendering the instant art area highly unpredictable.

F. The amount of direction provided by the applicant: The instant disclosure provides only two examples wherein the effect of po-ATP is disclosed as being effective in the inhibition of the cell growth of only one a cell line: human umbilical venous endothelial cells (HUVEC). No additional data is presently of record to support the extrapolation of this data to the instant claimed subject matter wherein o-ATP is administered in combination with a vast array of different classes of medicinally active ingredients to treat a vast array of disease conditions including all possible diseases classified as a "cancer" listed in claim **3** and one of the neoplastic diseases (leukemia) listed in claim **4**.

G. The existence of working examples: Only two working examples have been provided in the disclosure as described in the preceding paragraph. Additional data has been supplied by the declaration filed June 17, 2008 by applicant/Mme. Ferrero.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because of the absence of sufficient test data and associated guidance. The absence of sufficient test data means that the ordinary practitioner does not have the guidance necessary to practice the vast array of different disease treatments without undue experimentation.

Applicant's arguments filed January 12, 2009 have been fully considered but they are not persuasive.

Applicant has argued that "Ehrlich tumor cells" are not an example of a lymphoma. Examiner respectfully disagrees and cites a result of a newly executed Google search in support of this view (see PTO-892 ref. **U**).

In addition, applicant argues that the newly supplied declaration provides adequate support for the conclusion that the newly amended claims are adequately enabled by the original disclosure when supplemented by the declaration. Examiner respectfully disagrees, noting the absence of a clear showing that the claimed subject matter is actually included within the scope of either lymphomas or VEGF inhibitor treated diseases. Examiner also notes that the **Cory et al** reference citation of "Ehrlich tumor cells" is apparently properly considered

a report of effective treatment of a lymphoma in view of the contents of newly supplied reference **U**, in contradiction of applicant's assertions to the contrary..

In view of the above arguments and the examiner response following the first rejection supra, examiner has concluded that the instant claims, while of considerably narrowed scope, still remain inadequately enabled in view of the entire factual picture presented by applicant.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **1, 9-10 and 14-15** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Cory et al.** (PTO-892 ref. **R**).

The **Cory et al.** reference discloses the effective inhibition of a neoplastic disease condition (Ehrlich tumor cells aka "lymphoma") in the abstract and at page 818, column 1, Table 1, last two entries. According to one source ("Ehrlich tumor cells" search on the WEB via Google) are a variety of "lymphoma." Therefore, the instant claimed subject matter is deemed to have been anticipated.

Applicant's arguments filed January 12, 2009 have been fully considered but they are not persuasive.

Applicant has argued that "Ehrlich tumor cells" are not lymphoma cells. Examiner respectfully disagrees with applicants's unsupported assertion and directs applicant's attention to the newly cited PTO-892 ref. **U** wherein a Google search of the internet has produced clear evidence to the contrary.. Therefore, the above rejection has been maintained.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **1, 9-10 and 14-15** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Cory et al.** (PTO-892 ref. **R**).

The instant claims are directed to the administration of
-- po-ATP -- for the treatment of diseases wherein "VEGF-induced cell division" occurs and has permitted the development of a blood supply and the vessels necessary for same, and also for treatment of the associated neoplasm or other disease.

The **Cory et al.** reference discloses the effective inhibition of a neoplastic disease condition (Ehrlich tumor cells; e.g. a variety of lymphoma) in the abstract and at page 818, column 1, Table 1, last two entries.

Cory et al. does not expressly disclose the treatment of any other neoplastic disease condition.

The disclosure of the effective treatment of a disease specified at least generically by the instant claims, by a compound well known in the prior art, implies that the mechanism of this treatment, while not specifically disclosed in the prior art, was the effect responsible for the prior art report. Therefore, the instant cited prior art renders obvious from some to all of the claimed treatments of neoplasms and other diseases wherein po-ATP is the active ingredient.

Therefore, the instant claimed methods of treatment of disease conditions wherein VEGF induces tissue blood supply availability, typically in the development of neoplastic tissue

growth, would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments filed January 12, 2009 have been fully considered but they are not persuasive.

Applicant is referred to the response following the previous rejection.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
01/20/2009

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